REMARKS

Claims 2-19 and 22-31 are pending in the subject application. Applicants have not added, amended, or cancelled any claim herein.

Summary of February 10, 2011 telephone Examiner Interview

On February 10, 2011 a telephone Examiner Interview was conducted concerning the subject application among Examiner Sznaidman, Adam C. Krol of the undersigned's office and the undersigned. Applicants submit this Summary pursuant to 37 C.F.R. § 1.133(b). Applicants acknowledge with appreciation the courtesy that Examiner Sznaidman extended during the February 10, 2011 interview.

Applicants requested the February 10, 2011 interview to discuss the Amendment in Response to July 6, 2010 Office Action and Declaration of Dr. Jacob Bar-Tana ("Declaration") submitted January 6, 2011 in connection with the subject application.

At the beginning of the interview Examiner Sznaidman made applicants aware that a Final Office Action had been prepared although it had not yet been posted on PAIR. Despite this information applicants proceeded to discuss with the Examiner the Amendment and the Declaration submitted January 6, 2011 as well as pending claims 11 and 22-31.

During the February 10, 2011 interview, applicants explained that the Declaration shows that the claimed dose ranges of 3,3,14,14-tetramethyl hexadecane-1,16-dioic acid ("M16") to treat dyslipoproteinemia produces an unexpected result.

Examiner Sznaidman indicated that in his opinion the data in Table 1 of the Declaration did not show an unexpected result. Specifically, the Examiner stated that no conclusions can be drawn from the data presented in Table 1 because Table 1 does not show data from a single group of patients each administered doses of M16 from 30-600 mg/day. The Examiner also stated that the data presented in Table 1 does not show an unexpected result because the data for each individual patient shows a decrease in triglyceride levels with each increasing dose of M16 administered. The Examiner indicated that his rationale is set forth in detail in the Final Office Action.

In response, applicants then directed the Examiner's attention to Table 2 of the Declaration indicating Table 2 shows that the dose range of M16 which is maximally effective to treat dylipoproteinemia is unexpectedly different from the dose range of M16 which is maximally effective to treat insulin resistance, and that this difference shows that the claimed dose range is nonobvious. Examiner Sznaidman indicated that he had questions about the data in Table 2, and suggested it would be desirable to hold a follow-up interview in which the inventor, Dr. Bar-Tana, would participate to further explain the data presented in the Declaration.

Summary of March 24, 2011 telephone Examiner Interview

On March 24, 2011 a telephone Examiner Interview was conducted concerning the subject application among Examiner Sznaidman, Dr. Jacob Bar-Tana, Michal Hackmey (applicants' Israeli patent attorney), Adam C. Krol, and the undersigned. Applicants submit this Summary pursuant to 37 C.F.R. § 1.133(b). Applicants acknowledge with appreciation the courtesy that Examiner Sznaidman extended during the March 24, 2011 interview.

Applicants requested the March 24, 2011 interview to discuss the February 10, 2011 Final Office Action issued in connection with the subject application, and pending claims 11 and 22-31 were specifically discussed.

Applicants presented reasons warranting a finding of patentability of the above-identified claims, which applicants explain in detail below. Briefly, applicants explained that (i) the cited prior art does not teach or suggest the claimed dose range of M16 for the treatment of any condition, let alone dyslipoproteinemia, (ii) the data disclosed in the cited prior art which was obtained in studies of normolipemic rats cannot be the basis for an extrapolation as to the treatment of dyslipoproteinemia in a non-normolipemic (or hyperlipemic) human, and (iii) the Declaration of Dr. Bar-Tana shows an unexpected result.

Examiner Sznaidman agreed that applicants had made good points and agreed to reconsider the grounds for rejection in the February 10, 2011 Final Office Action upon submission of a written response.

Claims Rejected Under 35 U.S.C. § 103(a)

In the February 10, 2011 Final Office Action, the Examiner rejected claims 11 and 22-31 under 35 U.S.C. 103(a) as unpatentable over Bar-Tana 1 (U.S. Patent No. 6,303,653) and Bar-Tana 2 (U.S. Patent No. 6,284,903).

The Examiner asserted that Bar-Tana 1 teaches a method of treating Syndrome X by administering a therapeutically effective amount of M16. The Examiner acknowledged that Bar-Tana 1 "does

not teach the dose range from about 30 mg per day to about 400 mg per day" as recited in claim 11 or the dose ranges recited in claims 22-24 and claims 30-31. See, February 10, 2011 Final Office Action, page 5.

The Examiner further asserted that Bar-Tana 2 teaches that M16 is effective in reducing total cholesterol and plasma triglycerides "which offers an adequate treatment mode for combined hypertriglyceridemia-hypercholesterolemia." See, February 10, 2011 Final Office Action, page 5. The Examiner further asserted that Bar-Tana 2 teaches a daily dosage of 50-5000 mg, which will depend on the age, needs and tolerance of the individual patient.

The Examiner further asserted that dose range of Bar-Tana 2 clearly overlaps with the dose ranges of the instant claims. Citing M.P.E.P. § 2144.05, the Examiner stated that in the case where the claimed ranges overlap or lie inside ranges disclosed in the prior art, a *prima facie* case of obviousness exists. The Examiner then asserted that it would have been obvious to one skilled in the art to optimize the dose regimen based on age, tolerance, and the individual needs of the patient as taught by Bar-Tana 2, to obtain applicants' claimed invention with a reasonable expectation of success.

Applicants' Response

In response, applicants traverse the rejection for the reasons which follow.

A. Neither Bar-Tana 1 nor Bar-Tana 2 teach or suggest the use of applicants' claimed dose range of M16 for the treatment of dyslipoproteinemia

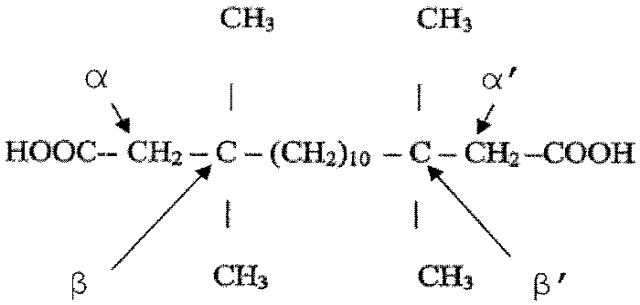
Bar-Tana 1

The Examiner acknowledged on page 5 of the February 10, 2011 Final Office Action that Bar-Tana 1 does not teach the dose range of "about 30 mg per day to about 400 mg per day" recited in claim 11. Importantly, Bar-Tana 1 does not teach any M16 dose or dose range for treating either Syndrome X, let alone any component disease such as dyslipoproteinemia. Bar-Tana 1 also does not teach that different dose ranges of M16 are or would be maximally effective to treat different component diseases of Syndrome X, implying that the same dosage will be effective to treat each such component disease, including dyslipoproteinemia and insulin resistance.

Bar-Tana 2

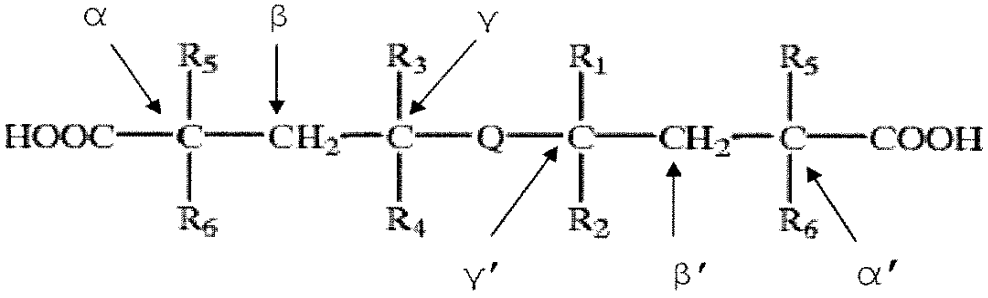
Bar-Tana 2 also does not teach any dose or dose range of M16 effective for treating dyslipoproteinemia or any other disease, let alone a maximally effective dose range. The 50-5000 mg dose range disclosed in Bar-Tana 2 and cited in the February 10, 2011 Final Office Action is for compounds of "formula (I)" which does not encompass M16. See, Bar-Tana 2, column 4, lines 64-67 ("[t]he daily dosage of the compounds of formula (I)...will usually range from 50 mg to from 5,000 mg per day"). Emphasis added.

Applicants respectfully direct the Examiner's attention to page 7 of the subject application, where the structure of M16 is shown. For the Examiner's convenience, an annotated version of the structure of M16 is reproduced below.



M16

As shown in the above annotated structure, M16 is a β,β′-methyl substituted α,ω-dicarboxylic acid. In contrast, the compounds of formula (I) of Bar-Tana 2 are <u>not</u> β,β′-methyl substituted. An annotated version of the structure of formula (I) shown in column 1 of Bar-Tana 2 is reproduced below.



As shown in the above annotated structure, the compounds of formula (I) are not β,β′-methyl substituted, but are substituted only on the alpha and/or gamma position. Thus, M16 is not a compound of formula (I). Accordingly, Bar-Tana 2 does not teach any dose or dose range of M16 for treating dyslipoproteinemia.

B. The data of Tables II and III of Bar-Tana 2 cannot be the basis for an extrapolation as to the treatment of dyslipoproteinemia

The data of Tables II and III of Bar-Tana 2 were obtained after feeding normolipemic rats a diet supplemented with M16, γ,γ'-methyl substituted α,ω-hexadecanedioic acid or α,α'-methyl substituted α,ω-hexadecanedioic acid. See, Bar-Tana 2, column 5. Lowering triglyceride ("TG") levels in normolipemic rats by administering M16 cannot be equated with reducing TG in hypertriglyceridemic animals, and certainly does not predict, with a reasonable likelihood of success, an effective treatment of a human patient with hyper-triglyceridemia, let alone dyslipoproteinemia.

Importantly, plasma TG level reflects the net balance between triglyceride production (by the liver, followed by secretion to plasma) and TG clearance (by consumption in muscle, adipose fat, etc.). The effect of lowering plasma TG in normolipemic animals due to enhancement of TG clearance rate can be totally masked in hyperlipemic animals in which TG production surpasses the respective increase in TG clearance rate. For decreasing plasma TG in the hyperlipemic animal, one would have to inhibit TG production rate. Accordingly, the data of Tables II and III of Bar-Tana 2 obtained from normolipemic rats is not a basis for predicting that M16 will be effective to treat dyslipoproteinemia.

C. The January 6, 2011 Declaration of Dr. Bar-Tana shows an unexpected result

The triglyceride data in the previously submitted Declaration establishes a trend and shows that the maximal effective dose for reducing elevated triglycerides is 200 mg/day. Specifically, doses of 30-200 mg/day decreased triglycerides by 42-53% from baseline, while dose escalation to 400 mg/day provided essentially the same decrease and did not produce any further significant decrease. See, Declaration, page 3 and Table 1.

In contrast, the data in Table 2 of the Declaration shows that a 200 mg/day dose of M16 (the maximal effective dose for lowering triglycerides) resulted in a non-significant increase in sensitization to insulin. See, Declaration, page 5 and Table 2. This result could not have been expected in view of the teachings of Bar-Tana 1 and Bar-Tana 2 because Bar-Tana 1 and Bar-Tana 2 do not suggest any maximally effective dose for treating Syndrome X, let alone the maximal effective dose of M16 which would be useful to treat different component diseases of Syndrome X.[1]

In summary, applicants' argument is as follows:

1. There is no dose range disclosed in Bar-Tana 1 or Bar-Tana 2 for treating any condition. Therefore, applicants' claimed dose range is not overlapping with any disclosed range and is not obvious;
2. There is no basis for extrapolating from the data in normolipemic rats in Bar-Tana 2 that M16 would be effective to treat dyslipoproteinemia in a human patient suffering therefrom; and

1 Tables 1 and 2 of the Declaration show data for the same six subjects who received the 200 mg/day dose of M16.

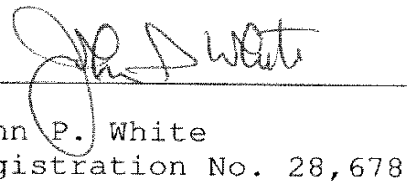
3. The data in the previously submitted Declaration of Dr. Bar-Tana establishes the unexpected result obtained with applicants' claimed dosage range in treating dyslipoproteinemia.

Each of the precedent arguments is individually sufficient to overcome the Examiner's rejection under 35 U.S.C. § 103, therefore applicants request that the Examiner reconsider and withdraw the rejection set forth in the February 10, 2011 Final Office Action.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

No fee is deemed necessary in connection with the filing of this Response. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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4/6/11

Adam C. Krol Date
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